

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s): Kushner, Peter J.; Webb, Paul; Williard, Renee; Hunt, C. Anthony; and Lopez, Gabriella

Assignee: The Regents of the University of California

Title: Methods for Screening Compounds for Estrogenic Activity

Serial No.: To be assigned Filing Date: Herewith

Examiner: To be assigned Group Art Unit: To be assigned

Docket No.: M-8963-2 US

San Jose, California
December 4, 2000

BOX PATENT APPLICATION
COMMISSIONER FOR PATENTS
Washington, D. C. 20231

PRELIMINARY AMENDMENT PURSUANT TO 37 C.F.R. 1.121

Dear Sir:

Please enter the following Preliminary Amendment in the above identified patent application filed herewith before calculating claim fees. This application is filed as a 37 C.F.R. § 1.53(b) divisional of co-pending U.S. Application No. 08/930,455, filed January 12, 1998 which is a National Phase filing under 35 U.S.C. §371 of PCT Application PCT/US96/04104, filed March 26, 1996, which is a continuation-in-part of U.S. Application No. 08/410,807, filed March 27, 1995, which is a continuation-in-part of U.S. Application No. 08/115,161, filed September 1, 1993. Claims pending in this application after entry of this Amendment are provided in Appendix I for the Examiner's convenience.

IN THE SPECIFICATION

At page 1, please delete lines 4-6 and substitute therefor the following:

--This non-provisional application is filed under 37 C.F.R. § 1.53(b) as a divisional of co-pending U.S. Application No. 08/930,455, filed January 12, 1998 which is a National Phase filing under 35 U.S.C. §371 of PCT Application PCT/US96/04104, filed March 26, 1996, which is a continuation-in-part of U.S. Application No. 08/410,807, now U.S. Patent No. 5,723,291 filed March 27, 1995, which is a continuation-in-part of now abandoned U.S.

Application No. 08/115,161, filed September 1, 1993 all of which are incorporated herein by reference in their entirety for all purposes.--

IN THE CLAIMS

Please cancel claims 27-29 without prejudice. Please amend claims 2-12, 14-17, 19-22 and 24-26 as follows:

Claims 2-6, 8, 10, and 12, line 1, respectively, please delete "(a)" and substitute therefor --1--.

Claim 7, please delete "claim 5" and substitute therefor --claim 6--.

Claim 9, please delete "claim 7" and substitute therefor --claim 8--.

Claim 11, please delete "claim 9" and substitute therefor --claim 10--.

Claims 14-17, line 1, respectively, delete "claim 12" and substitute therefor --claim 13--.

Claims 19-22, line 1, respectively, delete "claim 17" and substitute therefor --claim 18--.

Claims 24-26, line 1, respectively, delete "claim 22" and substitute therefor --claim 23--.

REMARKS

Status

Claims 1-29 are pending in this application, no claims being added, claims 2-12, 14-17, 19-22 and 24-26 being amended and claims 27-29 are canceled herewith. The parent application was subject to a restriction requirement (Paper Number 9, mailed March 8, 1999) and Applicants initially elected to prosecute Claim Group VII (original claims 27-29) with traverse. Claims 1-26 are pending in this application and represent the non-elected claims from the previous restriction requirement. Claims 2-6, 8, 10 and 12 are amended to correct formal deficiencies and claims 7, 9, 11, 14-17, 19-22, and 24-26 are amended to correct claim dependencies. This Amendment introduces no new matter.

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In the specification.

The specification is amended to correctly recite the priority of this application. No new matter is added by this Amendment.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (415) 217-6022.

EXPRESS MAIL LABEL NO:

EL707914877US

Respectfully submitted,

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APPENDIX I

CLAIMS PENDING AS OF DECEMBER 4, 2000

1. A method for screening a test compound for the ability to activate transcription through an indirect estrogen response, the method comprising:
 - a) providing a cell comprising an estrogen receptor and a promoter comprising an AP1 site which regulates expression of a reporter gene;
 - b) contacting the cell with the test compound; and
 - c) detecting the expression of the reporter gene.
2. (Amended) A method of claim 1, wherein the cell is an Ishikawa cell.
3. (Amended) A method of claim 1, wherein the cell over-expresses the estrogen receptor.
4. (Amended) The method of claim 1, wherein the promoter is genetically engineered to comprise an AP1 site.
5. (Amended) The method of claim 1, wherein the test compound is known to have antiestrogenic activity.
6. (Amended) The method of claim 1, wherein the cell is derived from uterine tissue.
7. (Amended) The method of claim 6, wherein the cell is a HeLa cell or an Ishikawa cell.
8. (Amended) A method of claim 1, further comprising the steps of:
 - a) providing a second cell comprising an estrogen receptor and a promoter comprising a standard estrogen response element which regulates expression of a second reporter gene;
 - b) contacting the second cell with the test compound; and

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c) detecting the expression of the second reporter gene.

9. (Amended) A method of claim 8, wherein the response element is from the *Xenopus* vitellogenin A2 gene.

10. (Amended) A method of claim 1, wherein the cell further comprises a promoter comprising a standard estrogen response element which regulates expression of second reporter gene.

11. (Amended) A method of claim 10, wherein the response element is from the *Xenopus* vitellogenin A2 gene.

12. (Amended) An estrogen agonist identified by the method of claim 1.

13. A method for screening a test compound for the ability to inhibit transcription through an indirect estrogen response, the method comprising:

- a) providing a cell comprising an estrogen receptor and a promoter comprising an AP1 site which regulates expression of a reporter gene;
- b) contacting the cell with the test compound an a compound known to mediate an indirect estrogen response;
- c) detecting the expression of the reporter gene.

14. (Amended) The method of claim 13, wherein the compound is known to mediate an indirect estrogen response is tamoxifen.

15. (Amended) A method of claim 13, wherein the cell over-expresses the estrogen receptor.

16. (Amended) The method of claim 13, wherein the promoter is genetically engineered to comprise an AP1 site.

17. (Amended) A compound identified by the method of claim 13.

18. A method for screening a test environmental compound for estrogenic activity, the method comprising:

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a) providing a cell comprising an estrogen receptor and a promoter comprising an estrogen response element which regulates the expression of a reporter gene;

b) contacting the cell with the test compound; and

c) detecting the expression of the reporter gene.

19. (Amended) The method of claim 18, wherein the cell further comprises a promoter comprising an AP1 site which regulates expression of a second reporter gene.

20. (Amended) The method of claim 18, wherein the reporter gene is CAT.

21. (Amended) The method of claim 18, wherein the cell over-expresses the estrogen receptor.

22. (Amended) The method of claim 18, wherein the cell is an ERC1 cell.

23. A method of inhibiting agonistic activity of an antiestrogen compound, said method comprising administering with said antiestrogen compound an inhibitor selected from the group consisting of genistein, staurosporine, 6-thioguanine, and 2 aminopurine.

24. (Amended) The method of claim 23, wherein said inhibiting agonistic activity comprises inhibiting an indirect estrogen response.

25. (Amended) The method of claim 23, wherein said antiestrogen compound is tamoxifen.

26. (Amended) The method of claim 23, wherein said inhibition is *in vivo*.

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